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Short communication

New lower nicotine cigarettes can produce compensatory smoking and increased carbon monoxide exposure

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Abstract

Potential reduced exposure products (PREPs) are marketed as a means to reduce exposure to tobacco toxicants. Quest® cigarettes, a new type of PREP, use genetically modified tobacco to provide a nicotine step-down approach, and are available as 0.6, 0.3 and 0.05 mg nicotine cigarettes. However, these cigarettes deliver equivalent levels of tar (10 mg). Prior research on low nicotine cigarettes suggests smokers will compensate for lower nicotine delivery by increasing their puffing behavior to extract more nicotine. This study tested the hypothesis that compensatory smoking will occur with this PREP as nicotine levels decrease, increasing exposure to tobacco toxins. Fifty smokers completed a within-subject human laboratory study investigating the effect of cigarette nicotine level on smoking behavior. Cigarette nicotine level was double-blinded and order of presentation counter-balanced. Breath carbon monoxide (CO) boost was used as a biomarker of smoke exposure; total puff volume to assess smoking behavior. Total puff volume was greatest for the 0.05 mg nicotine cigarette and CO boost was moderately greater after smoking the 0.3 and 0.05 mg cigarettes compared to the 0.6 mg nicotine cigarette. These data provide novel behavioral and biochemical evidence of compensatory smoking when smoking lower nicotine cigarettes. Although marketed as a PREP, increases in CO boost suggest this product can potentially be a harm-increasing product.

Keywords: Nicotine; Puff volume; Topography; Carbon monoxide

1. Introduction

The Institute of Medicine (IOM) report on tobacco harm reduction defines a product as harm reducing if it lowers total tobacco related mortality and morbidity, even though use of that product may involve continued exposure to tobacco-related toxicants (Stratton et al., 2001a,b). The IOM concludes that products that actually reduce harm may be a feasible and justifiable public health policy, particularly for those who cannot or will not quit smoking (Stratton et al., 2001a). However, careful evaluation of these potential reduced exposure products (PREPs) is necessary to characterize reductions in exposure to harmful substances, and to determine if there is an association between reduced exposure and reduced harm to health (Hatsukami et al., 2005; Stratton et al., 2001b).

One type of PREP, called Quest® (Vector Tobacco Inc., Durham, NC), uses genetically modified tobacco with lower nicotine levels to provide a means for smokers to "enjoy smoking by choosing to reduce your level of nicotine" (http://www.questcigs.com). Quest® cigarettes are manufactured with three progressively lower nicotine levels (0.6, 0.3, and 0.05 mg) and marketed as allowing smokers to "step-down" nicotine levels to "nicotine-free smoking" (http://www.questcigs.com). However, each of the three levels of Quest® cigarettes deliver equivalent levels of tar (10 mg) during standardized testing, and thus, are likely to pose health risks (Thun and Burns, 2001).

Nicotine is the primary addictive agent in cigarettes (United States Department of Health and Human Services (USDHHS, 1988)), and previous research has shown that smokers will alter their smoking behavior when switched to "light" cigarettes with lower delivery of nicotine (Benowitz et al., 1983; Zacny and Stitzer, 1988). By taking larger and more frequent puffs, a smoker can extract more nicotine from a "light" cigarette, and is

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consequently exposed to more tar from the smoke particulates that contain 81 known carcinogenic compounds (Hoffmann and Hecht, 1990; Smith et al., 2003). How a cigarette is smoked is referred to as smoking topography, and includes such measures as the number of puffs, puff volume, duration, and velocity (Bridges et al., 1986; Kolonen et al., 1992; USDHHS, 1988).

Altering smoking topography to offset a lower nicotine cigarette is a mechanism called compensation, and includes taking bigger puffs, taking more puffs, and smoking more cigarettes per day (Kozlowski et al., 2000; Scherer, 1999). Studies of "light" cigarettes show that smokers are able to extract more nicotine, tar and carbon monoxide (CO) from a cigarette than the standard levels reported by the Federal Trade Commission (FTC) (Benowitz et al., 2005; FTC Report, 2000, Scherer, 1999). However, unlike "light" cigarettes, smokers who use Quest® cigarettes may not be able to increase their nicotine levels through compensation due to the genetically modified tobacco not containing nicotine. Little is known about whether changes in smoking topography occur when smokers switch to this new low nicotine product. Since smoking topography can determine, in part, overall exposure to CO (Hofer et al., 1992; Zacny et al., 1987) and tobacco carcinogens (Djordjevic et al., 2000) characterizing topography and exposure with these new cigarette products is an important first step toward understanding associated health risks.

We conducted a within-subject human laboratory study to investigate the effect of cigarette nicotine level (0.6, 0.3, and 0.05 mg) on smoking topography and carbon monoxide exposure. We hypothesized that compensatory smoking, specifically greater total puff volume, would be observed as nicotine levels decreased, thereby supporting behavioral compensation. Further, due to increased total puff volume, we hypothesized increases in CO boost as nicotine levels decreased (i.e. biochemical evidence of compensation).

2. Methods

2.1. Participant recruitment

Smokers responding to community-based flyers were screened for eligibility via telephone. Inclusion criteria were: over age 18, smoke at least 10 daily cigarettes, smoking for a minimum 5 years, not currently trying to quit smoking, and report inhaling when smoking. Participants were excluded if they did not meet each of the inclusion criteria; reported trying to quit smoking, including current use of nicotine replacement therapy; or reported consuming more than 25 alcohol drinks per week. No participants had previously used Quest® cigarettes. Participants completed the single session experiment between March and August 2005 and were paid $100.00 for completing the entire study.

Sixty-nine people called the research center and 61 were eligible to participate. Ineligibility was due to smoking too few cigarettes ($n = 4$), trying to quit smoking ($n = 2$) and consuming more than 25 alcohol drinks per week ($n = 2$). Of the 61 eligible participants, eight refused to participate (not interested, time commitment too great); 53 scheduled an appointment. Three people missed their scheduled appointment time and 50 completed the single session.

2.2. Procedures

The study protocol was approved by the University Institutional Review Board. Experimental sessions were run between 8:00 and 16:00 h, and lasted approximately 3.5 h. Participants were required to bring a pack of their own cigarettes and were informed that they would smoke one of their own cigarettes and three other cigarettes with varying levels of nicotine during the session. They were instructed to abstain from cigarettes and caffeinated products for 1 h, and alcohol for 12 h, prior to attending the experimental session. Participants were encouraged to eat prior to attending the session and eating was not permitted between cigarettes.

Upon arrival to the laboratory, participants were seated in a comfortable chair in an observation room equipped with a smoke filtration system, and permitted to read or watch television when not smoking. After providing consent, breath alcohol content and baseline exhaled breath CO samples were collected, along with self-report questionnaires including demographic information, smoking history and general mood measures.

All cigarettes were smoked using the CReSS (Clinical Research Support System) smoking topography machine (Plowshare, Baltimore, MD). This device has been previously used in our laboratory to assess smoking behavior (Strasser et al., 2004, 2005), and has been shown to be a valid and reliable means to measure smoking behavior (Lee et al., 2003). Cigarettes are placed in a mouthpiece attached to an air-filled tube which leads to a pressure transducer. The device converts pressure changes during puffing into a digital signal. Sterilization of mouthpieces and unit calibration were performed prior to each session and by the guidelines of the manufacturer.

Participants had the smoking topography equipment explained to them and then were asked to smoke one of their own brand cigarette through the device. This permitted the participant to get accustomed to the smoking topography and CO devices and to standardize the time since last cigarette.

Thirty minutes after smoking their own brand cigarette, participants smoked the first of three Quest® cigarettes. The researcher instructed participants when to light each cigarette and a 30-min interval between cigarettes was timed from when the cigarette was extinguished to the lighting of the next cigarette. The Quest® cigarettes were presented in randomized order, counter-balanced across participants to minimize potential order effects. Quest® cigarettes were masked and color-coded so that participant and researcher were blind to nicotine level but able to distinguish between cigarettes by color. Color code was randomly generated and a study staff member who did not conduct sessions prepared the cigarettes.

Prior to, and 4 min after smoking each cigarette, participants provided breath CO samples. To obtain consistent readings, participants were instructed to inhale deeply, hold their breath for 2 s, then exhale, inhale again, hold their breath for 15 s and then exhale as long as possible in the CO breath sample device (Vitalograph, Lenexa, KS). The highest reading displayed on the digital screen, in parts per million (ppm), was recorded. Upon extinguishing each cigarette, participants completed a 14-item subjective rating of the cigarette they had just finished smoking.

2.3. Measures

2.3.1. Covariates. Covariates included age, sex, body mass index based on measured height and weight, nicotine level of preferred brand cigarette, and nicotine dependence (Fagerstrom Test for Nicotine Dependence, FTND; Heatherton et al., 1991).

2.3.2. Primary outcome: smoking topography. The smoking topography device employs a pressure transducer that measures pressure changes during puffing. Pressure changes are amplified, digitized and sampled at 1000 Hz and software converts signal to airflow (ml/s) in real time (s), which is subsequently converted to puff number, puff volume, puff duration, puff velocity and interpuff interval. The primary topography measure utilized for the current study was total puff volume, the sum of the volumes of all puffs taken while consuming the cigarette. Total puff volume was selected because it would provide a metric to quantify smoke exposure; permit comparison between nicotine levels and between participants; provide evidence of compensation; while allowing flexibility to account for individual differences in compensatory smoking behavior, such as taking more puffs and/or larger puff volumes. Total puff volume allows participants to compensate in different ways, a necessity demonstrated by Benowitz et al. (2005).

2.3.3. Secondary outcome: carbon monoxide. Participants provided two breath CO samples prior to, and 4 min after smoking each cigarette. Pairs of readings were averaged to determine pre-cigarette CO level and post-cigarette CO level. The difference between the pre- and post-cigarette readings was calculated as the measure of CO boost (Strasser et al., 2005; Zacny et al., 1987).

2.3.4. Subjective cigarette ratings. To assess subjective responses related to taste and flavor, participants completed a rating scale of cigarette features. The measure uses a 100 mm visual analog scale with descriptive anchors and participant instructions are to: place a vertical line at the location that best represents their rating of the cigarette for each characteristic. Items include: strength, harshness, heat, draw, taste (bad/good), satisfaction, burn rate, taste (mildness), too mild, harshness of smoke, after taste, staleness, strength of smoke, and smoke smell (pleasantness). These items have been used previously to assess subjective ratings of cigarettes (Strasser et al., 2005). At the conclusion of the session, participants were asked which color cigarette had the most and least amount of nicotine.

2.4. Statistical methods

Recruitment of 50 participants was determined as an appropriate sample size based on effect sizes (ES = 0.4) from similar smoking topography and CO boost studies (Strasser et al., 2004, 2005), with alpha set to 0.05 for a two-tailed test, and to provide greater than 80% power to detect between-cigarette nicotine level differences in total puff volume and CO boost.

Analyses were conducted using SPSS 12.0 (SPSS, Chicago, IL). Descriptive statistics were used to characterize the participant population in terms of demographic and smoking history variables. Associations between descriptive statistics and baseline CO and CO boost of own cigarette were tested by correlation analysis for continuous variables and analysis of variance (ANOVA) for nominal variables in order to identify potential confounds.

Repeated measures ANOVA was used to test for effects of cigarette nicotine levels on total puff volume, CO boost, and subjective ratings, and to test for potential order effects. Covariates were included in the analyses and those with significance levels of $p > 0.15$ were removed from the model. Bonferroni post hoc analyses with an alpha conservatively set to 0.0167 (0.05/3) were performed to compare differences between specific pairs of nicotine levels only after significant main effects were observed.

3. Results

3.1. Descriptive statistics

All 50 participants (54% male) who entered the study completed the single session. The participant sample was White (72%) and Black (24%), Native American (2%) and Asian American (2%); 4% identified themselves as Hispanic, irrespective of race. Thirty percent of participants were college graduates and 90% had completed high school. Participant mean body mass index (BMI; kg/m^2) was 26.7 (S.D. = 5.4, range 18.9–40.2, BMI $\geq$ 30, $n = 12$). Participants were on average 44.5 (S.D. = 12.1, range 22–72) years of age, reported smoking 21.3 (S.D. = 8.1, range 10–40) daily cigarettes, and have smoked daily for 27.8 (S.D. = 12.6, range 6–59) years. Their mean FTND nicotine dependence score was 5.5 (S.D. = 1.9, range 2–10). Participant preferred brand was varied; the most prevalent included: Marlboro Regular (24%), Marlboro Light (12%), USA (10%), Winston (8%), Camel (4%), Parliament (4%), and GPC (4%). Half of participants preferred cigarette type was Regular; 48% was Light; 2% was Ultra-Light. Mean standard nicotine level was 0.94 mg nicotine (S.D. = 0.3) and mean standard tar was 12.9 mg (S.D. = 8.7; FTC Report, 2000). None of the participants smoked unfiltered cigarettes. All participants had a breath alcohol content reading equal to 0.000 at the beginning of the session.

3.2. Baseline CO and CO boost from preferred brand cigarette

Mean CO level at baseline, prior to smoking own cigarette was 24.4 ppm (S.D. = 12.3, range 1.0–58.0). The participant with baseline CO = 1.0 ppm reported having not smoked for the previous 15 h, but did report typically smoking 10 daily cigarettes and had a nicotine dependence score of 4. Mean CO boost of own cigarette was 5.5 ppm (S.D. = 2.64, range 0.5–10.0). Start time of sessions varied between 08:00 and 16:00 and was not associated with baseline CO ($r = 0.09$, $p = 0.52$) or CO boost of own cigarette ($r = -0.01$, $p = 0.96$).

Associations between participant characteristics and baseline CO levels were explored to identify potential confounds to include in the analyses of nicotine level on total puff volume and CO boost. Self reported number of daily cigarettes smoked was significantly associated with baseline CO ($r = 0.56$, $p < 0.01$). Sex, nicotine dependence, preferred cigarette type, years smoked, and BMI were not associated with baseline CO ($p > 0.15$).

Neither the participant with baseline CO = 1 ppm nor the participant with CO boost of own cigarette equal to 0.5 ppm affected significance for analyses of association when excluded. Therefore both were included in all further analyses. Order of cigarette presentation had no effect on smoking topography or CO boost.

3.3. Outcome measure: smoking topography

Mean total puff volume measures were 570.5 ml (S.D. = 156.9), 518.1 ml (S.D. = 145.6), and 540.3 ml (S.D. = 144.9) for the 0.05 mg nicotine, 0.3 mg nicotine and 0.6 mg nicotine cigarettes, respectively [$F(2, 47) = 5.73$, $p = 0.006$]. Self-reported number of daily cigarettes was the single significant covariate remaining in the model. Post hoc Bonferroni analyses indicate that total puff volume for the 0.05 mg nicotine cigarette was statistically greater than total puff volume of the 0.3 mg nicotine cigarette ($p = 0.0013$), and had a trend toward being significantly greater than the total puff volume of the 0.6 mg nicotine cigarette ($p = 0.049$). Smoking topography measures are presented in Table 1 and (Fig. 1).

3.4. Outcome measure: carbon monoxide boost

Mean CO boost measures were 5.3 ppm (S.D. = 2.5), 5.8 ppm (S.D. = 2.6), and 4.7 ppm (S.D. = 2.7) for the 0.05 mg nicotine, 0.3 mg nicotine and 0.6 mg nicotine cigarettes, respectively [$F(2, 47) = 5.43$, $p = 0.01$]. Self-reported number of daily cigarettes was the single significant covariate remaining in the model. Post hoc Bonferroni analyses indicate that CO boost for the 0.3 mg nicotine cigarette was significantly greater than the 0.6 mg nicotine cigarette ($p = 0.007$). Values for CO boost for own cigarette and Quest® cigarettes are presented in Table 1 and (Fig. 1).

Table 1
CO boost, smoking topography and subjective ratings of own brand and three nicotine levels of Quest® cigarettes

	Cigarette type (mg of nicotine)			
	Own brand (various)	Quest® 1 (0.6 mg)	Quest® 2 (0.3 mg)	Quest® 3 (0.05 mg)
Biochemical measure				
CO boost (ppm)	5.5 (4.8–6.3)	4.7 (4.0–5.5)	5.8 (5.1–6.6)	5.3 (4.6–6.0)
Smoking topography measures				
Total puff volume (ml)	832.0 (737–926)	540.3 (500–580)	518.1 (478–558)	570.5 (527–614)
Number of puffs	14.3 (12.8–15.7)	9.8 (9.0–10.5)	9.9 (8.9–10.9)	10.0 (9.1–10.9)
Puff duration (s)	1.8 (1.6–1.9)	1.8 (1.6–1.9)	1.7 (1.5–1.8)	1.8 (1.6–1.9)
Puff volume (ml)	60.5 (55.2–65.7)	58.1 (53.3–62.8)	55.9 (51.0–60.8)	59.4 (54.6–64.3)
Puff velocity (ml/s)	35.5 (22.3–37.8)	34.5 (32.0–37.0)	34.4 (31.9–37.0)	35.1 (32.5–37.8)
Interpuff interval (s)	21.6 (19.1–24.1)	21.6 (19.0–24.2)	19.6 (16.9–22.3)	18.6 (15.7–21.6)
Subjective ratings				
Strength-very weak/very strong	60.7 (53.7–67.8)	44.4 (38.4–50.5)	40.3 (32.9–47.6)	28.3 (21.1–35.6)
Harshness-very mild/very harsh	29.6 (23.3–35.9)	33.7 (27.3–40.1)	35.9 (28.1–43.7)	27.8 (20.2–35.4)
Heat-no heat/very hot	19.0 (13.7–24.2)	24.5 (18.9–30.1)	27.6 (20.2–35.1)	26.4 (19.6–33.2)
Draw-easy/difficult	46.5 (7.8–85.2)	26.3 (19.9–32.7)	46.9 (8.1–85.6)	28.3 (20.8–35.8)
Taste-very bad/very good	70.0 (62.7–78.0)	44.6 (30.1–43.6)	36.8 (30.1–43.6)	53.3 (14.7–91.8)
Satisfaction from smoking-unsatisfying/satisfying	70.3 (62.7–78.0)	44.3 (36.3–52.2)	36.8 (29.3–44.3)	24.4 (18.3–30.5)
Burned/did not burn too fast in too few puffs	86.7 (49.4–100.0)	26.0 (19.3–32.7)	22.3 (17.0–27.6)	21.8 (15.5–28.2)
Mild taste/not mild taste	46.7 (38.8–54.7)	33.2 (26.3–40.2)	35.5 (27.8–43.2)	33.2 (25.5–41.0)
It was/was not too mild for me	71.4 (64.0–78.8)	42.4 (33.5–51.4)	41.1 (31.7–50.5)	31.4 (23.0–39.8)
Smoke seemed/did not seem harsh	75.3 (68.8–81.8)	56.2 (47.7–64.8)	57.6 (48.9–66.3)	61.6 (52.6–70.5)
Did not leave/left a good aftertaste in my mouth	54.1 (45.5–62.7)	59.7 (21.3–98.1)	35.0 (27.4–42.5)	44.4 (5.6–83.1)
Somehow it seemed/did not seem stale	84.1 (79.1–89.1)	59.4 (51.5–67.3)	58.0 (49.9–66.1)	53.7 (44.4–63.0)
Smoke seemed very weak/very strong	62.4 (55.4–69.4)	44.6 (37.7–51.4)	37.8 (30.8–44.8)	31.9 (24.2–39.5)
Smoke smell-unpleasant/pleasant	65.0 (58.4–71.6)	50.2 (43.1–57.3)	48.4 (41.4–55.3)	46.0 (39.4–52.7)

Data presented as mean (±95% confidence interval).

3.5. Subjective measures and identifying nicotine levels

Strength of cigarette, satisfaction from smoking, and smoke strength differed significantly by nicotine level ($p < 0.01$). The 0.6 mg nicotine cigarette was rated as stronger, more satisfying, and its smoke reported as most strong compared to the other Quest® cigarettes. The 0.05 mg nicotine cigarette was rated the lowest on each of these subjective ratings. Values for all subjective measures for participant own brand and Quest® cigarettes are presented in Table 1.

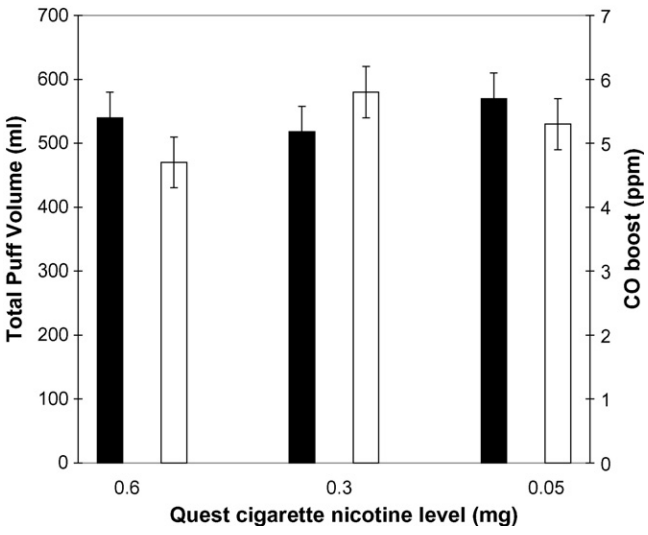

Fig. 1. The effect of cigarette nicotine level on total puff volume [(ml; solid bars; left *y*-axis); $F(2, 47) = 5.73$, $p = 0.006$, $N = 50$] and mean carbon monoxide boost [(ppm; open bars; right *y*-axis); $F(2, 47) = 5.43$, $p = 0.01$, $N = 50$]. Data presented as mean (±95% confidence interval).

At the conclusion of the session participants were asked which color cigarette had the most and least nicotine. Fifty four percent correctly identified the 0.6 mg nicotine cigarette as the highest nicotine cigarette. Only 12% stated the 0.05 mg nicotine cigarette had the highest nicotine level. Fifty-eight percent correctly identified the 0.05 mg nicotine cigarette as the least nicotine-containing cigarette; 18% incorrectly identified the 0.6 mg nicotine cigarette as the lowest. Only 38% correctly identified both the 0.6 mg nicotine cigarette and the 0.05 mg nicotine cigarette. Ability to discriminate nicotine levels did not affect total puff volume or CO boost. However, those participants who correctly discriminated cigarette nicotine levels rated the 0.6 mg nicotine cigarette as strongest and most satisfying and the 0.05 mg nicotine as least strong and satisfying, while the non-discriminators reported no subjective differences by nicotine level.

4. Discussion

This study provides novel behavioral and biochemical evidence for the potential of compensatory smoking with a new low nicotine cigarette product, supporting the potential for increased, rather than reduced, harm from this PREP. As hypothesized, both total puff volume and CO boost per cigarette increased when cigarette nicotine level decreased, although the effect was modest. Subjective ratings of cigarette strength and satisfaction

were significantly lower for the lower nicotine cigarettes, ratings of other cigarette features (e.g., draw and taste) were very similar across nicotine levels, consistent with evidence that tar levels contribute to the ability to discriminate cigarettes (Schuh et al., 2001). The non-significant results for most cigarette rating items are important because most brand-switching studies find several subjective and sensory differences by cigarette type (Pickworth et al., 1999; Rose et al., 1993; Strasser et al., 2005; Zacny et al., 1987), likely attributable, in part, to non-nicotine differences between the cigarettes. A true test of compensatory smoking attributable to nicotine levels should use cigarettes that are identical in tar levels and design characteristics, such as filter ventilation levels, draw and taste (Scherer, 1999).

These findings extend previous investigations of compensation when smokers switched to cigarette brands with lower nicotine and tar yields based on standardized testing (Benowitz, 2001; Zacny et al., 1987). However, the lower nicotine cigarettes tested in previous studies had design features that would permit smokers to extract more nicotine from the cigarette by increasing puffing or by occluding filter ventilation holes (Jarvis et al., 2001; Rickert et al., 1983). Quest® cigarettes contain equivalent levels of tar, do not appear to be ventilated, and nicotine delivery is restricted due to the use of genetically modified, nicotine-free tobacco. However, since smokers are unlikely to be aware of, or fully understand, these design differences, compensatory smoking behavior is still likely to occur.

Compensatory smoking behavior and increased CO boost was not a ubiquitous occurrence, although total puff volume at the 0.3 mg nicotine and 0.05 mg nicotine levels were significantly correlated ($r = 0.60$, $p < 0.001$); as was CO boost ($r = 0.93$, $p < 0.001$). Overall, effect sizes of cigarette nicotine level on total puff volume and CO boost were modest. However, for some participants the effect was notable. Twenty percent of participants exhibited 20% or greater increase in total puff volume [mean 42.5% (S.D. = 20.1)] when smoking the 0.05 mg nicotine cigarette compared to the 0.6 mg nicotine cigarette; 12% had 20% or greater increase in total puff volume [mean 41.5% (S.D. = 14.5)] for the 0.3 mg nicotine cigarette compared to smoking the 0.6 mg nicotine cigarette. Forty two percent of participants had 20% or greater increase in CO boost [mean 290% (S.D. = 452)] at 0.05 mg nicotine cigarette compared to 0.6 mg nicotine cigarette; 44% had a 20% or greater CO boost increase [mean 269% (S.D. = 515)] for 0.3 mg nicotine cigarette compared to 0.6 mg nicotine cigarette. This study was designed to be a preliminary investigation for evidence of compensatory smoking of a new PREP product, and was not designed or powered to identify subgroup differences. Future research on PREPs should attempt to characterize subgroups of those most prone to increased harm exposure from PREP products.

Participants smoked their preferred own brand as the first cigarette in order to permit them to become accustomed to the smoking topography device and to standardize the time since the last cigarette prior to smoking the Quest® cigarettes. Comparison of total puff volume and CO boost between preferred own brand and Quest® cigarettes is problematic due to the variation in participants' cigarette brands. However, it is noteworthy that: all standard nicotine levels of participants' preferred brand was greater than the highest nicotine Quest® (0.6 mg nicotine) cigarette; total puff volume when smoking preferred own brand cigarettes was greater than for any of the Quest® cigarettes; CO boost for preferred brand was similar to the lowest nicotine level Quest® cigarettes. Filter ventilation in the preferred own brand cigarettes can dilute the concentration of smoke, such that similar CO boost is observed although total puff volume of own brand is greater than for Quest® cigarettes. However, due to Quest® having less available nicotine, smokers potentially may use relatively more Quest® cigarettes daily.

Smoking topography has been used as an index of systemic smoke exposure from conventional cigarettes (Zacny et al., 1987) and proposed reduced exposure products (Breland et al., 2002; Buchhalter et al., 2001; Lee et al., 2004). Total puff volume, the metric chosen for the analysis of the present study, is a particularly informative index of systemic exposure (CO or nicotine boost); Burling et al. (1985), Gust and Pickens (1982) and Zacny et al. (1987) identified puff volume as an important determinant of tobacco exposure.

Ample evidence exists for the effect of smoking topography on carbon monoxide exposure (Hofer et al., 1992; USDHHS, 1988; Zacny et al., 1987) and support exists for its effect on carcinogen exposure (Djordjevic et al., 2000). Studies assessing exposure to multiple smoking-attributable biomarkers report significant, positive correlations between carbon monoxide levels and biomarkers of known carcinogens (Hecht et al., 2004; Joseph et al., 2005); specifically, 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol (NNAL) and 1-hydroxypyrene (1-HOP) are biomarkers of the carcinogen 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK) and of polycyclic aromatic hydrocarbons (PAHs), respectively. Further evidence for the relationship between smoking topography and carcinogen exposure is suggested by changes in carcinogen yield per cigarette as a result of compensatory smoking when daily cigarette consumption is reduced (Murphy et al., 2004), and when smokers are switched to a lower nicotine cigarette for an extended duration (Benowitz et al., 2005).

The present line of research should also be extended to include the measurement of additional biomarkers of harm. Research has shown that not all cigarette compounds change at the same rate as a function of compensatory smoking in cigarettes (Harris, 2004) and during PREP usage (Hatsukami et al., 2004). CO boost is a practical measure to use in this study because of its sensitivity to smoking during a single cigarette. However, extended use of Quest® would permit inclusion of other biomarkers of exposure that are better indicators of carcinogen exposure, such as NNK (4-methylnitrosamino-1-(3-pyridyl)-1-butanone) and 1-HOP (1-hydroxypyrene) uptake (Hecht, 1999; Hecht et al., 2004).

Smokers' perceptions of the features of new PREPs may also play an important role in determining smoking behavior with these products. As such, it is therefore important to understand how smokers interpret the explicit and implicit claims made in product marketing (Stratton et al., 2001b). Of particular relevance to the present findings is evidence that a substantial proportion of smokers make false inferences about the safety of Quest® cigarettes based on the Quest® advertise-

ment (Shadel et al., 2006). Smokers who switch to lower tar cigarettes, rather than quitting, often perceive that the cigarettes marketed by such advertisements are safer or healthier than regular cigarettes (Hamilton et al., 2004; Shiffman et al., 2004). Analyses of tobacco industry documents suggest that deliberate attempts have been made to create misunderstanding of health risk (Dunsby and Bero, 2004). If a novel cigarette product is misperceived as harm reducing, it possesses the risk of attracting cigarette smokers who otherwise would have quit or who would have adopted validated less harmful nicotine products.

There are a few limitations to our study. Participants smoked only one cigarette of each nicotine level. Based on the evidence for compensation when smoking a single cigarette, future investigations of smoking topography and CO boost when smoking lower nicotine cigarettes over a longer period of time are warranted. Extended observation of smoking behavior using Quest® cigarettes would also permit assessing multiple biomarkers of harm exposure. It is also possible that smokers who switch to Quest® cigarettes to reduce their nicotine exposure may increase their daily consumption of cigarettes (Benowitz, 2001). As a result, they may administer more daily nicotine when smoking Quest® than when smoking their own brand. Replication of results, characterization of prone subgroups, and investigation of long-term use of Quest® is necessary.

The present study makes an important first step in understanding the behavioral and biochemical effects of new lower nicotine cigarettes that have conventional tar levels. Evidence for behavioral compensation and increased CO exposure with lower nicotine cigarettes is particularly important in light of evidence that smokers infer from marketing claims that these cigarettes are less harmful (Shadel et al., 2006).

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